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☐	L4	l1 same human	8
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☐	L1	CD4+ CD25+	42

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 NEWS 4  JAN 13  IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS 5  JAN 13  New IPC 8 SEARCH, DISPLAY, and SELECT enhancements
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 NEWS 6  JAN 17  Pre-1988 INPI data added to MARPAT
 NEWS 7  JAN 17  IPC 8 in the WPI family of databases including WPIFV
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 NEWS 10  FEB 22  The IPC thesaurus added to additional patent databases on
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 NEWS 11  FEB 22  Updates in EPFULL; IPC 8 enhancements added
 NEWS 12  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS 13  FEB 28  MEDLINE/LMEDLINE reload improves functionality
 NEWS 14  FEB 28  TOXCENTER reloaded with enhancements
 NEWS 15  FEB 28  REGISTRY/ZREGISTRY enhanced with more experimental
spectral
          property data
 NEWS 16  MAR 01  INSPEC reloaded and enhanced
 NEWS 17  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 18  MAR 08  X.25 communication option no longer available after June
2006
 NEWS 19  MAR 22  EMBASE is now updated on a daily basis
 NEWS 20  APR 03  New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 21  APR 03  Bibliographic data updates resume; new IPC 8 fields and IPC
          thesaurus added in PCTFULL
 NEWS 22  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS 23  APR 12  LINSPEC, learning database for INSPEC, reloaded and
enhanced
 NEWS 24  APR 12  Improved structure highlighting in FQHIT and QHIT display
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 NEWS 25  APR 12  Derwent World Patents Index to be reloaded and enhanced
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          second quarter; strategies may be affected

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L1       6002 CD4 (3A) CD25

=> s l1 and human
L2       3060 L1 AND HUMAN

=> s l2 and CTL4A
L3          0 L2 AND CTL4A

=> s l2 and CTLA 4
L4       288 L2 AND CTLA 4

=> s l2 and CD153
L5          0 L2 AND CD153

=> s l2 and CD154
L6       13 L2 AND CD154

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L10        16 DUP REM L9 (18 DUPLICATES REMOVED)

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L10  ANSWER 1 OF 16  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN                          DUPLICATE 1
AN   2001208374  EMBASE
TI   A role for TGF-.beta. in the generation and expansion of  ***CD4*** (+)
     ***CD25*** (+) regulatory t cells from  ***human***  peripheral blood.
AU   Yamagiwa S.; Gray J.D.; Hashimoto S.; Horwitz D.A.
CS   Dr. D.A. Horwitz, Div. of Rheumatology and Immunology, University of
     Southern California, Keck School of Medicine, 2011 Zonal Avenue, Los
     Angeles, CA 90033, United States. dhorwitz@hsc.usc.edu
SO   Journal of Immunology, (15 Jun 2001) Vol. 166, No. 12, pp. 7282-7289. .
     Refs: 49
     ISSN: 0022-1767  CODEN: JOIMA3
CY   United States
DT   Journal; Article
FS   026    Immunology, Serology and Transplantation
LA   English
SL   English
ED   Entered STN: 28 Jun 2001
     Last Updated on STN: 28 Jun 2001
AB   An elusive goal in transplanting organs across histocompatibility barriers
     has been the induction of specific tolerance to avoid graft rejection.  A
     considerable body of evidence exists that the thymus produces regulatory T
     cells that suppress the response of other T cells to antigenic
     stimulation.  We report that TGF-.beta. can induce certain CD4(+) T cells
     in the naive (CD45RA(+)RO(-)) fraction in  ***human***  peripheral blood
     to develop powerful, contact-dependent suppressive activity that is not
     antagonized by anti-TGF-.beta. or anti-IL-10 mAbs.  The costimulatory
     effects of TGF-.beta. on naive CD4(+) T cells up-regulated CD25 and
     ***CTLA*** - ***4***  expression, increased their transition to the
     activated phenotype, but decreased activation-induced apoptosis.
     Suppressive activity was concentrated in the CD25(+) fraction.  These
     ***CD4*** (+) ***CD25*** (+) regulatory cells prevented CD8(+) T cells
     from proliferating in response to alloantigens and from becoming cytotoxic
     effector cells.  Moreover, these regulatory cells exerted their
     suppressive activities in remarkably low numbers and maintained these
     effects even after they are expanded.  Once activated, their suppressive
     properties were Ag nonspecific.  Although <1% of naive  ***CD4*** (+) T
     cells expressed  ***CD25*** , depletion of this subset before priming
     with TGF-.beta. markedly decreased the generation of suppressive activity.
     This finding suggests that  ***CD4*** (+) ***CD25*** (+) regulatory T
     cells induced ex vivo are the progeny of thymus-derived regulatory T cells
     bearing a similar phenotype.  The adoptive transfer of these regulatory T
     cells generated and expanded ex vivo has the potential to prevent
     rejection of allogeneic organ grafts.

L10  ANSWER 2 OF 16  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN                          DUPLICATE 2
AN   2001207649  EMBASE
TI   Ex vivo isolation and characterization of  ***CD4*** (+) ***CD25***
     (+) T cells with regulatory properties from  ***human***  blood.
AU   Dieckmann D.; Plottner H.; Berchtold S.; Berger T.; Schuler G.
CS   G. Schuler, Department of Dermatology, University of Erlangen-Nuremberg,
```

Hartmannstrasse 14, 91052 Erlangen, Germany. schuler@derma.med.uni-erlangen.de
SO Journal of Experimental Medicine, (4 Jun 2001) Vol. 193, No. 11, pp. 1303-1310. .
Refs: 29
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 10 Jul 2001
Last Updated on STN: 10 Jul 2001
AB It has been known for years that rodents harbor a unique population of ***CD4*** (+) ***CD25*** (+) "professional" regulatory/suppressor T cells that is crucial for the prevention of spontaneous autoimmune diseases. Here we demonstrate that ***CD4*** (+) ***CD25*** (+)CD45RO(+) T cells (mean 6% of CD4(+) T cells) are present in the blood of adult healthy volunteers. In contrast to previous reports, these ***CD4*** (+) ***CD25*** (+) T cells do not constitute conventional memory cells but rather regulatory cells exhibiting properties identical to their rodent counterparts. Cytotoxic T lymphocyte-associated antigen (***CTLA***)- ***4*** (CD152), for example, which is essential for the in vivo suppressive activity of ***CD4*** (+) ***CD25*** (+) T cells, was constitutively expressed, and remained strongly upregulated after stimulation. The cells were nonproliferative to stimulation via their T cell receptor for antigen, but the anergic state was partially reversed by interleukin (IL)-2 and IL-15. Upon stimulation with allogeneic (but not syngeneic) mature dendritic cells or platebound anti-CD3 plus anti-CD28 the ***CD4*** (+) ***CD25*** (+) T cells released IL-10, and in coculture experiments suppressed the activation and proliferation of CD4(+) and CD8(+) T cells. Suppression proved IL-10 independent, yet contact dependent as in the mouse. The identification of regulatory ***CD4*** (+) ***CD25*** (+) T cells has important implications for the study of tolerance in man, notably in the context of autoimmunity, transplantation, and cancer.

L10 ANSWER 3 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3
AN 2001207648 EMBASE
TI ***Human*** ***CD25*** (+) ***CD4*** (+) T regulatory cells suppress naive and memory T cell proliferation and can be expanded in vitro without loss of function.
AU Levings M.K.; Sangregorio R.; Roncarolo M.-G.
CS M.-G. Roncarolo, San Raffaele Telethon Institute, Via Olgettina 58, Milan 20132, Italy. m.roncarolo@hsr.it
SO Journal of Experimental Medicine, (4 Jun 2001) Vol. 193, No. 11, pp. 1295-1301. .
Refs: 23
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 10 Jul 2001
Last Updated on STN: 10 Jul 2001
AB Active suppression by T regulatory (Tr) cells plays an important role in the downregulation of T cell responses to foreign and self-antigens. Mouse CD4(+) Tr cells that express CD25 possess remarkable suppressive activity in vitro and in autoimmune disease models in vivo. Thus far, the existence of a similar subset of ***CD25*** (+) ***CD4*** (+) Tr cells in humans has not been reported. Here we show that ***human*** ***CD25*** (+) ***CD4*** (+) Tr cells isolated from peripheral blood failed to proliferate and displayed reduced expression of CD40 ligand (CD40L), in response to T cell receptor-mediated polyclonal activation, but strongly upregulated cytotoxic T lymphocyte-associated antigen (***CTLA***)- ***4*** . ***Human*** ***CD25*** (+) ***CD4*** (+) Tr cells also did not proliferate in response to allogeneic antigen-presenting cells, but they produced interleukin (IL)10, transforming growth factor (TGF)-.beta., low levels of interferon (IFN)-.gamma., and no IL-4 or IL-2. Importantly, ***CD25*** (+) ***CD4*** (+) Tr cells strongly inhibited the proliferative responses of both naive and memory CD4(+) T cells to alloantigens, but neither IL-10, TGF-.beta., nor ***CTLA*** - ***4*** seemed to be directly required for their suppressive effects. ***CD25*** (+) ***CD4*** (+) Tr cells could be expanded in vitro in the presence of IL-2 and allogeneic feeder cells and maintained their suppressive capacities. These findings that ***CD25*** (+) ***CD4*** (+) Tr cells with immunosuppressive effects can be isolated from peripheral blood and expanded in vitro without loss of function represent a major advance towards the therapeutic use of these cells in T cell-mediated diseases.

L10 ANSWER 4 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 4
AN 2001207647 EMBASE
TI Identification and functional characterization of ***human*** ***CD4*** (+) ***CD25*** (+) T cells with regulatory properties isolated from peripheral blood.
AU Jonuleit H.; Schmitt E.; Stassen M.; Tuettenberg A.; Knop J.; Enk A.H.
CS H. Jonuleit, Dept. of Dermatology, University of Mainz, D-55101 Mainz, Germany. jonuleit@hautklinik.klinik.uni-mainz.de
SO Journal of Experimental Medicine, (4 Jun 2001) Vol. 193, No. 11, pp. 1285-1294. .
Refs: 23
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 10 Jul 2001
Last Updated on STN: 10 Jul 2001
AB A subpopulation of peripheral ***human*** ***CD4*** (+) ***CD25*** (+) T cells that expresses CD45RO, histocompatibility leukocyte antigen DR, and intracellular cytotoxic T lymphocyte-associated antigen (***CTLA***) ***4*** does not expand after stimulation and markedly suppresses the expansion of conventional T cells in a contact-dependent manner. After activation, ***CD4*** (+) ***CD25*** (+) T cells express ***CTLA*** - ***4*** on the surface detectable for several weeks. These cells show a G1/G0 cell cycle arrest and no production of interleukin (IL)-2, IL-4, or interferon (IFN)-.gamma. on either protein or mRNA levels. The anergic state of ***CD4*** (+) ***CD25*** (+) T cells is not reversible by the addition of anti-CD28, anti- ***CTLA*** - ***4*** , anti-transforming growth factor .beta., or anti-IL-10 antibody. However, the refractory state of ***CD4*** (+) ***CD25*** (+) T cells was partially reversible by the addition of IL-2 or IL-4. These data demonstrate that ***human*** blood contains a resident T cell population with potent regulatory properties.

L10 ANSWER 5 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 5
AN 2001150762 EMBASE
TI ***Human*** ***CD4*** (+) ***CD25*** (+) thymocytes and peripheral T cells have immune suppressive activity in vitro.
AU Stephens L.A.; Mottet C.; Mason D.; Powrie F.
CS L.A. Stephens, Sir William Dunn School of Pathology, South Parks Road, Oxford OX1 3RE, United Kingdom. leighs@molbiol.ox.ac.uk
SO European Journal of Immunology, (2001) Vol. 31, No. 4, pp. 1247-1254. .
Refs: 27
ISSN: 0014-2980 CODEN: EJIMAF
CY Germany
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
048 Gastroenterology
LA English
SL English
ED Entered STN: 10 May 2001
Last Updated on STN: 10 May 2001
AB ***CD4*** (+) ***CD25*** (+) T cells in mice and rats are capable of transferring protection against organ-specific autoimmune disease and colitis and suppressing the proliferation of other T cells after polyclonal stimulation in vitro. Here we describe the existence in humans of ***CD4*** (+) ***CD25*** (+) T cells with the same in vitro characteristics. ***CD4*** (+)CD8(-) ***CD25*** (+) T cells are present in both the thymus and peripheral blood of humans (.apprx. 10% of CD4(+)CD8(-) T cells), proliferate poorly in response to mitogenic stimulation and suppress the proliferation of ***CD4*** (+) ***CD25*** (-) cells in co-culture. This suppression requires cell contact and can be overcome by the addition of exogenous IL-2. ***CD4*** (+) ***CD25*** (+) cells from thymus and blood were poor producers of IL-2 and IFN-.gamma., and suppressed the levels of these cytokines produced by ***CD4*** (+) ***CD25*** (-) cells. However, ***CD4*** (+) ***CD25*** (+) PBL produced higher levels of IL-4 and similar amounts of IL-10 as ***CD4*** (+) ***CD25*** (-) cells. Regulatory ***CD4*** (+) ***CD25*** (+) T cells have an activated phenotype in the thymus with expression of ***CTLA*** - ***4*** and CD122 (IL-2R.beta.). The fact that ***CD4*** (+) ***CD25*** (+) regulatory T cells are present with a similar frequency in the thymus of humans, rats and mice, suggests that the role of these cells in the maintenance of immunological tolerance is an evolutionarily conserved mechanism.

L10 ANSWER 6 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 6
AN 2001270500 EMBASE
TI ***CD4*** (+) ***CD25*** (high) regulatory cells in ***human*** peripheral blood.
AU Baecher-Allan C.; Brown J.A.; Freeman G.J.; Hafler D.A.
CS Dr. C. Baecher-Allan, Harvard Medical School, 77 Avenue Louis Pasteur, Boston, MA 02115, United States. callan@rics.bwh.harvard.edu
SO Journal of Immunology, (1 Aug 2001) Vol. 167, No. 3, pp. 1245-1253. .
Refs: 36
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 16 Aug 2001
Last Updated on STN: 16 Aug 2001
AB Thymectomy in mice on neonatal day 3 leads to the development of multiorgan autoimmune disease due to loss of a CD(+)CD25(+) T cell regulatory population in their peripheral lymphoid tissues. Here, we report the identification of a CD4(+) population of regulatory T cells in the circulation of humans expressing high levels of CD25 that exhibit in

vitro characteristics identical with those of the ***CD4*** (+) ***CD25*** (+) regulatory cells isolated in mice. With TCR cross-linking, ***CD4*** (+) ***CD25*** (high) cells did not proliferate but instead totally inhibited proliferation and cytokine secretion by activated ***CD4*** (+) ***CD25*** (-) responder T cells in a contact-dependent manner. The ***CD4*** (+) ***CD25*** (high) regulatory T cells expressed high levels of CD45RO but not CD45RA, akin to the expression of CD45RB(low) on murine ***CD4*** (+) ***CD25*** (+) regulatory cells. Increasing the strength of signal by providing either costimulation with CD28 cross-linking or the addition of IL-2 to a maximal anti-CD3 stimulus resulted in a modest induction of proliferation and the loss of observable suppression in cocultures of ***CD4*** (+) ***CD25*** (high) regulatory cells and ***CD4*** (+) ***CD25*** (-) responder cells. Whereas higher ratios of ***CD4*** (+) ***CD25*** (high) T cells are required to suppress proliferation if the PD-L1 receptor is blocked, regulatory cell function is shown to persist in the absence of the PD-1/PD-L1 or ***CTLA*** - ***4*** /B7 pathway. Thus, regulatory CD4 T cells expressing high levels of the IL-2 receptor are present in humans, providing the opportunity to determine whether alterations of these populations of T cells are involved in the induction of ***human*** autoimmune disorders.

L10 ANSWER 7 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 7
AN 2001318243 EMBASE
TI Oral tolerance: Immune mechanisms and the generation of Th3-type TGF-beta-secreting regulatory cells.
AU Weiner H.L.
CS H.L. Weiner, Department of Neurology, Harvard Med. Sch./Ctr. Neurol. Dis., Brigham and Women's Hospital, 77 Avenue Louis Pasteur, HIM 730, Boston, MA
02115-5817, United States. Weiner@cnd.bwh.harvard.edu
SO Microbes and Infection, (2001) Vol. 3, No. 11, pp. 947-954. .
Refs: 64
ISSN: 1286-4579 CODEN: MCINFS
CY France
DT Journal; General Review
FS 004 Microbiology
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
032 Psychiatry
LA English
SL English
ED Entered STN: 27 Sep 2001
Last Updated on STN: 27 Sep 2001
AB Oral tolerance is a long recognized method to induce peripheral immune tolerance. Oral tolerance has been used successfully to treat animal models of autoimmune diseases and is being tested in ***human*** diseases. Low doses of oral antigen induce active suppression, whereas high doses induce clonal anergy and deletion. Oral antigen preferentially generates a Th2(IL-4/IL-10)- or a Th3(TGF-.beta.)-type response. Th3-type cells are a unique T-cell subset which primarily secrete TGF-.beta., provide help for IgA and have suppressive properties for Th1 and other immune cells. Th3-type cells appear distinct from the Th2 cells as CD4(+) TGF-.beta.-secreting cells with suppressive properties in the gut have been generated from IL-4-deficient animals. In vitro differentiation of Th3-type cells from Th0 precursors from TCR transgenic mice is enhanced by culture with TGF-.beta., IL-4, IL-10 and anti-IL-12. Because regulatory T cells generated by oral antigen are triggered in an antigen-specific fashion but suppress in an antigen-nonspecific fashion, they mediate 'bystander suppression' when they encounter the fed autoantigen at the target organ. Thus, mucosal tolerance can be used to treat inflammatory processes that are not autoimmune in nature. Mucosal antigen has also been used to treat animal models of stroke and of Alzheimer's disease. Induction of low-dose oral tolerance is enhanced by oral administration of IL-4 and IL-10. Coupling antigen to CTB or administration of Flt-3 ligand enhances oral tolerance. Anti-B7.2 but not anti-B7.1 blocks low-dose, but not high-dose oral tolerance. High-dose oral tolerance is blocked by anti- ***CTLA*** - ***4*** . ***CD25*** (+) ***CD4*** (+) regulatory T-cell function also appears to be related to TFG-.beta.. .COPYRGT. 2001 Edition scientifiques et medicales Elsevier SAS.

L10 ANSWER 8 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 8
AN 2001373644 EMBASE
TI Unique chemotactic response profile and specific expression of chemokine receptors CCR4 and CCR8 by ***CD4*** (+) ***CD25*** (+) regulatory T cells.
AU Iellem A.; Mariani M.; Lang R.; Recalde H.; Panina-Bordignon P.; Sinigaglia F.; D'Ambrosio D.
CS Dr. D. D'Ambrosio, Roche Milano Ricerche, v. Olgettina 58, Milano 1-20132, Italy. daniele.dambrosio@roche.com
SO Journal of Experimental Medicine, (17 Sep 2001) Vol. 194, No. 6, pp. 847-853. .
Refs: 30
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 8 Nov 2001
Last Updated on STN: 8 Nov 2001
AB Chemokines dictate regional trafficking of functionally distinct T cell subsets. In rodents and humans, a unique subset of ***CD4*** (+) ***CD25*** (+) cytotoxic T lymphocyte antigen (***CTLA***)- ***4*** (+) regulatory T cells (Treg) has been proposed to control peripheral tolerance. However, the molecular basis of immune suppression and the trafficking properties of Treg cells are still unknown. Here, we determined the chemotactic response profile and chemokine receptor expression of ***human*** blood-borne ***CD4*** (+) ***CD25*** (+) Treg cells. These Treg cells were found to vigorously respond to several inflammatory and lymphoid chemokines. Treg cells specifically express the chemokine receptors CCR4 and CCR8 and represent a major subset
of circulating CD4(+) T cells responding to the chemokines macrophage-derived chemokine (MDC)/CCL22, thymus and activation-regulated
chemokine (TARC)/CCL17, I-309/CCL1, and to the virokine vMIP-I (ligands of CCR4 and CCR8). Blood-borne CD4(+) T cells that migrate in response to CCL1 and CCL22 exhibit a reduced alloproliferative response, dependent on the increased frequency of Treg cells in the migrated population. Importantly, mature dendritic cells preferentially attract Treg cells among circulating CD4(+) T cells, by secretion of CCR4 ligands CCL17 and CCL22. Overall, these results suggest that CCR4 and/or CCR8 may guide Treg cells to sites of antigen presentation in secondary lymphoid tissues and inflamed areas to attenuate T cell activation.

L10 ANSWER 9 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:493469 BIOSIS
DN PREV200100493469
TI Identification and functional characterization of ***human*** ***CD4*** + ***CD25*** + T-cells with regulatory properties isolated from peripheral blood.
AU Enk, A. [Reprint author]; Jonuleit, H. [Reprint author]; Schmitt, E.; Stassen, M.; Tuettenberg, A. [Reprint author]; Knop, J. [Reprint author]
CS Department of Dermatology, University of Mainz, Mainz, Germany
SO Journal of Investigative Dermatology, (***August, 2001***) Vol. 117, No. 2, pp. 455. print.
Meeting Info.: 62nd Annual Meeting of the Society for Investigative Dermatology. Washington, DC, USA. May 09-12, 2001.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002

L10 ANSWER 10 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 9
AN 2001375172 EMBASE
TI Regulation of surface and intracellular expression of ***CTLA*** - ***4*** on ***human*** peripheral T cells.
AU Wang X.-B.; Zheng C.-Y.; Giscombe R.; Lefvert A.K.
CS Prof. A.K. Lefvert, Immunological Research Unit, Ctr. for Molec. Med. (CMM) L8: 03, Karolinska Hospital, SE-171 76 Stockholm, Sweden. Ann.Kari.Lefvert@cmm.ki.se
SO Scandinavian Journal of Immunology, (2001) Vol. 54, No. 5, pp. 453-458. .
Refs: 30
ISSN: 0300-9475 CODEN: SJIMAX
CY United Kingdom
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 8 Nov 2001
Last Updated on STN: 8 Nov 2001
AB Cytotoxic T-lymphocyte-associated antigen (***CTLA*** - ***4***) is an important downregulator of T-cell activation. In order to analyze the expression and regulation of ***CTLA*** - ***4*** on ***human*** peripheral T cells, ***CTLA*** - ***4*** mRNA and protein expression were determined using analysis by reverse transcription-polymerase chain reaction (RT- PCR) and FACs, respectively. Intracellular ***CTLA*** - ***4*** was constitutively expressed in unstimulated CD4(+) and CD8(+) T cells. Interleukin (IL)-2 induced a dose-dependent increase of both intracellular and surface expression of ***CTLA*** - ***4*** (CD152). Most of the CD4(+) and CD8(+) cells expressing ***CTLA*** - ***4*** also expressed CD25. Interferon (IFN)-.gamma. induced the upregulation of ***CTLA*** - ***4*** expression via antigen-presenting cells (APC) activation. The CTLA-4delTM mRNA (550 bp) had a shorter half-life than the full length ***CTLA*** - ***4*** mRNA and the expression was downregulated upon activation of the cells by treatment with IL-2. Given an inhibitory role of ***CTLA*** - ***4*** and ***CD4*** (+) ***CD25*** (+) T cells in immune responses, the present findings suggest that IL-2-induced immunosuppression may result from its stimulatory effect of the ***CTLA*** - ***4*** expression.

L10 ANSWER 11 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on
STN
AN 2002:186742 BIOSIS
DN PREV200200186742
TI Increased immunoregulatory ***CD4*** + ***CD25*** + T cell subset and

CTLA - ***4*** expression in cord blood CD4+ T cells may contribute to the increased degree of tolerance following unrelated cord blood (UCBT) versus unrelated adult donor blood stem cell transplantation (UADSCT).

AU Liu, Zhuoru [Reprint author]; Son, Ni Huiping [Reprint author]; Cairo, Seth [Reprint author]; Vande Ven, Carmella [Reprint author]; Cairo, Mitchell S. [Reprint author]

CS Pediatric Oncology, Columbia University, New York, NY, USA

SO Blood, (***November 16, 2001***) Vol. 98, No. 11 Part 1, pp. 380a-381a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LA English

ED Entered STN: 13 Mar 2002
Last Updated on STN: 13 Mar 2002

AB We and others have demonstrated a lower incidence of severe (grade III/IV) AGVHD following UCBT compared to UADSCT (Cairo, et al, Blood 90:4665, 1997). The aim of this study is to understand the mechanisms underlying this clinical observation. ***CD4*** + ***CD25*** + T cells have been known in rodents and recently in ***human*** to be 'professional' regulatory/suppresor T cells. This subset of T cells expresses a higher level of the negative regulator of ***CTLA*** - ***4*** (Shevach, et al, JEM193:F41, 2001). In this study, we tested whether alloantigen stimulation induces the ***CD4*** + ***CD25*** + subset of T cells in cord blood (CB). CD4+ T cells were isolated by negative selection with a Dynal T cell isolation kit and CD8 Dynal beads from CB and adult peripheral blood (APB) mononuclear cells. They were stimulated with allogeneic antigen presenting cells (allo-APC) at 1 to 0.5 of responder/stimulator (R/S) ratio. The cultures were restimulated weekly at the same R/S ratio. IL-2 (20 units/ml) was added to the culture 3 days after restimultion. For the proliferation response, 5X104 T cells/well were cultured with 2.5X104 APC/well in 96-well round-bottomed plates. 3H thymidine was added after 5 days (MLR) or 48 h (3 day proliferation assay) culture. 3H thymidine incorporation was measured 18 h later. Expression of ***CTLA*** - ***4*** was determined by intracytoplasmic staining and flowcytometry analysis. Seven days after initial stimulation, the percentage of CD25+ cells in CB T cells was higher than that in APB T cells (34% and 8% respectively). Upon restimulation with the same APC, CB T cells exhibited a lower proliferation response (46+-8% of the response of APB T cells, n=5, p<0.001) and higher expression of ***CTLA*** - ***4*** (22% for CB and 5% for APB T cells). At the end of restimulation, the percentage of CD25+ cells remained higher in CB T cells (33% for CB and 9% for APB T cells). The proliferation response of these CB T cells further decreased (24+-11% of the response of APB T cells, n=5, p<0.001) and their expression of ***CTLA*** - ***4*** remained higher (36% for CB and 16% for APB T cells) after additional challenge with allo-APC. To test if there is a population of regulatory T cells, allostimulated CB and APB CD4+ T cells were added to MLR cultures of CB and APB naive CD4+ T cells against the APC. Preliminary results showed that allostimulated CB T cells suppressed the MLR of both CB and APB-T cells (47% and 46% of suppression respectively) at a 1 to 1 ratio of allostimulated T cell/responder naive T cell. Depletion of ***CD4*** + ***CD25*** + cells from allostimulated CB T cells abrogated this suppressive effect. Our data suggest that interaction of CB T cells with allo-APC induces a higher percentage of ***CD4*** + ***CD25*** + regulatory/suppressor T cells and increased expression of ***CTLA*** - ***4*** , which may in part contribute to an increased degree of tolerance and a decreased allograft effect potentially resulting in a lower incidence of severe AGVHD in UCBT vs. UADSCT.

L10 ANSWER 12 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2002:152766 BIOSIS

DN PREV200200152766

TI Identification of regulatory ***CD4*** + ***CD25*** + T cells following ***human*** stem cell transplantation.

AU Cobbold, Mark [Reprint author]; Ainsworth, Jenni [Reprint author]; Dunnion, Debbie [Reprint author]; Piper, Karen [Reprint author]; Fegan, Chris; Milligan, Don; Mahendra, Prem; Chakraverty, Ronjon [Reprint author]; Craddock, Charles; Moss, Paul [Reprint author]

CS CRC Institute for Cancer Studies, University of Birmingham, Birmingham, UK

SO Blood, (***November 16, 2001***) Vol. 98, No. 11 Part 2, pp. 324b. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

AB A subset of CD4+ T cells characterised by expression of CD25 and ***CTLA*** - ***4*** has been described in both murine and ***human*** studies and appears to act as an immune regulatory cell. This subset typically constitutes between 1 and 6% of the total CD4+ population and appears to exert a suppressive effect on the proliferative capacity of the ***CD4*** + ***CD25*** -population. How this effect is mediated is unknown but may involve both cell contact dependent and independent mechanisms. Regulatory T cells may play an important role in controlling alloreactive immune responses following stem cell transplantation. In murine models the depletion of ***CD4*** + ***CD25*** + cells impairs the development of immunological tolerance to tissue grafts. We have studied immune reconstitution in patients who have undergone allogeneic stem cell transplantation and have focussed on the levels and phenotype of ***CD4*** + ***CD25*** + T cells. ***CD4*** + ***CD25*** + T cell numbers were highly variable between patients but had a characteristic cellular phenotype. In some cases there was a significant increase in regulatory T cell numbers 6 months following allografting compared to pre-transplant levels. The functional properties of these cells and their clinical correlates are currently under investigation. ***CD4*** + ***CD25*** + regulatory T cells are a relatively novel functional subset of lymphocytes that may have a critical role to play in immune homeostasis following allografting.

L10 ANSWER 13 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

AN 2001408195 EMBASE

TI Control of T-cell activation by ***CD4*** (+) ***CD25*** (+) suppressor T cells.

AU Shevach E.M.; McHugh R.S.; Piccirillo C.A.; Thornton A.M.

CS E.M. Shevach, Laboratory of Immunology, Natl. Inst. of Allergy/Infect. Dis., Building 10, Bethesda, MD 20892, United States. ems1@mail.nih.gov

SO Immunological Reviews, (2001) Vol. 182, pp. 58-67. .
Refs: 35
ISSN: 0105-2896 CODEN: IMRED2

CY Denmark

DT Journal; General Review

FS 026 Immunology, Serology and Transplantation

LA English

SL English

ED Entered STN: 6 Dec 2001
Last Updated on STN: 6 Dec 2001

AB Depletion of the minor (.apprx.10%) subpopulation of CD4(+) T cells that co-expresses CD25 (interleukin (IL)-2 receptor .alpha.-chain) by thymectomy of neonates on the third day of life or by treatment of adult CD4(+) T cells with anti-CD25 and complement results in the development of organ-specific autoimmunity. Autoimmune disease can be prevented by reconstitution of the animals with ***CD4*** (+) ***CD25*** (+) cells. ***CD4*** (+) ***CD25*** (+)-mediated protection of autoimmune gastritis does not require the suppressor cytokines IL-4, IL-10, or transforming growth factor (TGF)-beta.. Mice that express a transgenic T-cell receptor (TCR) derived from a thymectomized newborn that recognizes the gastric parietal cell antigen H/K ATPase all develop severe autoimmune gastritis very early in life. ***CD4*** (+) ***CD25*** (+) T cells are also powerful suppressors of the activation of both CD4(+) and CD8(+) T cells in vitro. Suppression is mediated by a cell contact-dependent, cytokine-independent T-T interaction. Activation of ***CD4*** (+) ***CD25*** (+) via their TCR generates suppressor effector cells that are capable of non-specifically suppressing the activation of any CD4(+) or CD8(+) T cell. Activation of suppressor effector function is independent of co-stimulation mediated by CD28/ ***CTLA*** - ***4*** interactions with CD80/CD86. We propose that ***CD4*** (+) ***CD25*** (+) T cells recognize organ-specific antigens, are recruited to sites of autoimmune damage where they are activated by their target antigen, and then physically interact with autoreactive CD4(+) or CD8(+) effector cells to suppress the development of autoimmune disease.

L10 ANSWER 14 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

AN 2000323617 EMBASE

TI CD40 ligand (***CD154***) triggers a short-term CD4+ T cell activation response that results in secretion of immunomodulatory cytokines and apoptosis.

AU Blair P.J.; Riley J.L.; Harlan D.M.; Abe R.; Tadaki D.K.; Hoffmann S.C.; White L.; Francomano T.; Perfetto S.J.; Kirk A.D.; June C.H.

CS P.J. Blair, NIDDK-Navy Transplant./Autoimmun., Naval Medical Research Center, 8901 Wisconsin Ave., Bethesda, MD 20889-5607, United States. blairp@nmripo.nmri.nnmc.navy.mil

SO Journal of Experimental Medicine, (21 Feb 2000) Vol. 191, No. 4, pp. 651-660. .
Refs: 52
ISSN: 0022-1007 CODEN: JEMEAV

CY United States

DT Journal; Article

FS 026 Immunology, Serology and Transplantation

LA English

SL English

ED Entered STN: 28 Sep 2000
Last Updated on STN: 28 Sep 2000

AB Signals generated through CD28-B7 and CD40 ligand (CD40L)-CD40 interactions have been shown to be crucial for the induction of long-term allograft survivability. We have recently demonstrated that humanized anti-CD40L (hu5C8) prevents rejection of mismatched renal allografts in primates. To investigate potential mechanisms of CD40L-induced allograft acceptance, we coimmobilized hu5C8 with suboptimal amounts of anti-CD3 to stimulate CD4+ T cells. We now report that anti-CD3/CD40L costimulation results in CD28-independent activation and subsequent deletion of resting T cells. Coligation of CD3 and CD40L increased expression of CD69,

CD25 , and CD54 on ***CD4*** + T cells. We also found that costimulation with anti-CD3/CD40L resulted in enhanced production of interleukin (IL)-10, interferon .gamma., and tumor necrosis factor .alpha. but not IL-2 or IL-6. Interestingly, after several days, anti-CD3/CD40L-mediated activation was followed by apoptosis in a significant population of cells. Consistent with that observation, anti-CD3/CD40L did not enhance the antiapoptotic proteins Bcl-2 and Bcl-xL. Further, the addition of CD28 at 24 h failed to rescue those cells induced to die after costimulation with anti-CD3/CD40L. Together, these data suggest that the graft-sparing effect of hu5C8 in vivo may result in part from early and direct effects on CD4+ T cells, including a vigorous induction of immunomodulatory cytokines and/or apoptosis of allograft-specific T cells.

L10 ANSWER 15 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 10
AN 2000259066 EMBASE
TI Immunologic self-tolerance maintained by ***CD25*** + ***CD4*** + regulatory T cells constitutively expressing cytotoxic T lymphocyte-associated antigen 4.
AU Takahashi T.; Tagami T.; Yamazaki S.; Uede T.; Shimizu J.; Sakaguchi N.; Mak T.W.; Sakaguchi S.
CS S. Sakaguchi, Dept. of Experimental Pathology, Inst. for Frontier Medical Sciences, Kyoto University, 53 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan. shimon@frontier.kyoto-u.ac.jp
SO Journal of Experimental Medicine, (17 Jul 2000) Vol. 192, No. 2, pp. 303-309. .
Refs: 31
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 10 Aug 2000
Last Updated on STN: 10 Aug 2000
AB This report shows that cytotoxic T lymphocyte-associated antigen 4 (***CTLA*** - ***4***) plays a key role in T cell-mediated dominant immunologic self- tolerance. In vivo blockade of ***CTLA*** - ***4*** for a limited period in normal mice leads to spontaneous development of chronic organ-specific autoimmune diseases, which are immunopathologically similar to ***human*** counterparts. In normal naive mice, ***CTLA*** - ***4*** is constitutively expressed on ***CD25*** + ***CD4*** + T cells, which constitute 5-10% of peripheral CD4+ T cells. When the ***CD25*** + ***CD4*** + T cells are stimulated via the T cell receptor in vitro, they potently suppress antigen-specific and polyclonal activation and proliferation of other T cells, including ***CTLA*** - ***4*** -deficient T cells, and blockade of ***CTLA*** - ***4*** abrogates the suppression. CD28-deficient ***CD25*** + ***CD4*** + T cells can also suppress normal T cells, indicating that CD28 is dispensable for activation of the regulatory T cells. Thus, the ***CD25*** + ***CD4*** + regulatory T cell population engaged in dominant self-tolerance may require ***CTLA*** - ***4*** but not CD28 as a costimulatory molecule for its functional activation. Furthermore, interference with this role of ***CTLA*** - ***4*** suffices to elicit autoimmune disease in otherwise normal animals, presumably through affecting ***CD25*** + ***CD4*** + T cell-mediated control of self-reactive T cells. This unique function of ***CTLA*** - ***4*** could be exploited to potentiate T cell-mediated immunoregulation, and thereby to induce immunologic tolerance or to control autoimmunity.

L10 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:445290 BIOSIS
DN PREV200100445290
TI Immune response in coeliac disease: Involvement of costimulatory molecules during activation of lymphocytes infiltrating the intestine.
AU Witas, Henryk W. [Reprint author]; Mlynarski, Wojciech; Niewiadomska, Hanna; Socha, Jerzy; Rujner, Jolanta; Bodalski, Jerzy
CS Molecular Biology Unit, Institute of Pediatrics, Medical University, Sporna 36.50, 91-738, Lodz, Poland
witas@alef.am.lodz.pl
SO Central-European Journal of Immunology, (***2000***) Vol. 25, No. 4, pp. 180-184. print.
ISSN: 1426-3912.
DT Article
LA English
ED Entered STN: 19 Sep 2001
Last Updated on STN: 22 Feb 2002
AB The contribution of the costimulatory signal generated during intestinal T cell activation to the pathogenesis of coeliac disease (CD) was verified. Mucosal biopsy specimens obtained from CD patients with grade IV intestinal atrophy (n=10) and healthy control individuals (n=8) were subjected to immunohistochemistry assay using a LSAB plus PAP visualisation system. The studied CD subjects exhibited HLA DQA1 *0501-DQB1 *0201 haplotype. Immunocompetitive cells were phenotyped with antibodies against CD3, ***CD4*** , CD8, ***CD25*** , CD28, CD137, CD152 and TCR((. Observed intestinal lymphocytes were identified as two subpopulations i.e. infiltrating intraepithelial lymphocytes (IEL) and stromal lymphocytes (SL). 25.4% of IEL and 73.0% of SL exhibited CD4 in contrast to CD8 found on 67.0% of IEL and 23.5% of SL. A similar tendency was found for CD28 (34.5% and 74.8% for IEL and SL, respectively) and for CD137 (81.4% and 14.6%). There were no significant differences between the studied subjects concerning the SL subpopulation separately. However, when concerns IEL subpopulation, decreased ratio of CD28/CD152 in the CD group (0.072) as compared to controls (0.142) was observed. Similar differences were found for CD28/CD137 ratio (0.032 and 0.081, respectively). Moreover, TCRgammadelta were found in 18.3% IEL of CD patients versus 7.3% of controls. The results suggest that the costimulatory signal for lymphocyte activation provided with CD28, CD152 and CD137 molecules may contribute as a component of the immune response to intestinal atrophy in coeliac disease.

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 70.95 71.16

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LAST RELOADED: Apr 14, 2006 (20060414/UP).

=> FIL EMBASE BIOSIS CAPLUS
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FULL ESTIMATED COST 0.42 71.58

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=> s Schuler, G?/au
L11 1740 SCHULER, G?/AU

=> s l1 and l11
L12 13 L1 AND L11

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 7 DUP REM L12 (6 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 7 ANSWERS - CONTINUE? Y/(N):y

L13 ANSWER 1 OF 7 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1
AN 2005289512 EMBASE
TI Activated ***CD4*** (+) ***CD25*** (+) T cells suppress antigen-specific CD4(+) and CD8(+) T cells but induce a suppressive phenotype only in CD4(+) T cells.
AU Dieckmann D.; Plottner H.; Dotterweich S.; ***Schuler G.***
CS Dr. G. Schuler, Department of Dermatology, Univ. Hospital of Erlangen-Nuremberg, Hartmannstrasse 14, 91052 Erlangen, Germany. Gerold.Schuler@derma.imed.uni-erlangen.de
SO Immunology, (2005) Vol. 115, No. 3, pp. 305-314. .
Refs: 35
ISSN: 0019-2805 CODEN: IMMUAM
CY United Kingdom
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 21 Jul 2005
Last Updated on STN: 21 Jul 2005
AB ***CD4*** (+) ***CD25*** (+) regulatory T cells are increasingly recognized as central players in the regulation of immune responses. In vitro studies have mostly employed allogeneic or polyclonal responses to monitor suppression. Little is known about the ability of ***CD4*** (+) ***CD25*** (+) regulatory T cells to suppress antigen-specific immune responses in humans. It has been previously shown that ***CD4*** (+) ***CD25*** (+) regulatory T cells anergize CD4(+) T cells and turn them into suppressor T cells. In the present study we demonstrate for the first time in humans that ***CD4*** (+) ***CD25*** (+) T cells are able to inhibit the proliferation and cytokine production of antigen specific CD4(+) and CD8(+) T cells. This suppression only occurs when ***CD4*** (+) ***CD25*** (+) T cells are preactivated. Furthermore, we could demonstrate that CD4(+) T-cell clones stop secreting interferon-.gamma. (IFN-.gamma.), start to produce interleukin-10 and transforming growth factor-.beta. after coculture with preactivated ***CD4*** (+) ***CD25*** (+) T cells and become suppressive themselves. Surprisingly preactivated ***CD4*** (+) ***CD25*** (+)

T cells affect CD8(+) T cells differently, leading to reduced proliferation and reduced production of IFN-.gamma.. This effect is sustained and cannot be reverted by exogenous interleukin-2. Yet CD8(+) T cells, unlike CD4(+) T cells do not start to produce immunoregulatory cytokines and do not become suppressive after coculture with ***CD4*** (+) ***CD25*** (+) T cells. .COPYRGT. 2005 Blackwell Publishing Ltd.

L13 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:157515 CAPLUS
DN 140:198100
TI ***CD4*** + ***CD25*** - T cells and Tr1-like regulatory T cells induction and uses thereof in immunosuppression
IN ***Schuler, Gerold*** ; Dieckmann, Detlef
PA Germany
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1391504	A1	20040225	EP 2002-18025	20020812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004147021	A1	20040729	US 2003-618134	20030711
EP 1391210	A2	20040225	EP 2003-102508	20030812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI EP 2002-18025	A	20020812		
US 2002-419177P	P	20021017		

AB The disclosed invention provides ***CD4*** + ***CD25*** - T cells and Tr1-like regulatory T cells (i.e., contact-independent Type 1-like regulatory T cells), processes for their prodn., and their use for regulatory purposes. The above cells are induced following the co-culture of human ***CD4*** + ***CD25*** + T cells (+/+) with ***CD4*** + ***CD25*** - (+/-) T cells which leads to long-lasting anergy and interleukin-10 formation by +/- T cells. The +/- T cells anergized by the +/+ T cells subsequently suppress the activation of syngeneic CD4+ T cells in an interleukin-10-dependent manner. The +/- T cells or the Tr1-like regulatory T cells can be used for: prepn. of a regulatory medicament; in assays that will allow to identify other regulatory factors; for identifying mols. expressed by the +/- T cells (or the Tr1-like regulatory T cells) including identification of novel mols. on said cells; for identifying precursor cells or progeny of +/- T cells (or the Tr1-like regulatory T cells); and for prepg. an agent for adoptive transfer therapy, an agent for treating immune diseases, or an agent preventing/treating transplant rejections.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:714217 CAPLUS
DN 137:228962
TI ***CD4*** + ***CD25*** + regulatory T cells from human blood
IN ***Schuler, Gerold***
PA Germany
SO Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1241249	A1	20020918	EP 2001-106033	20010312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2441213	AA	20020919	CA 2002-2441213	20020312
WO 2002072799	A1	20020919	WO 2002-EP2671	20020312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1379625	A1	20040114	EP 2002-727397	20020312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002008076	A	20040302	BR 2002-8076	20020312
CN 1509327	A	20040630	CN 2002-809777	20020312
JP 2004529631	T2	20040930	JP 2002-571855	20020312
US 2005101012	A1	20050512	US 2003-661804	20030912
PRAI EP 2001-106033	A	20010312		
WO 2002-EP2671	W	20020312		

AB The present invention provides suppressive and/or regulative human ***CD4*** + ***CD25*** + T cells, a method for expanding same, and the use of the suppressive and/or regulative human ***CD4*** + ***CD25*** + T cells and the expanded T cells as regulatory agent.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:728268 CAPLUS
DN 139:259722
TI Human ***CD4*** + ***CD25*** + regulatory, contact-dependent T cells induce interleukin 10-producing, contact-independent type 1-like regulatory T cells. [Erratum to documents cited in CA137:123934, CA139:228952]
AU Dieckmann, Detlef; Bruett, Cord Henrik; Ploettner, Heidi; Lutz, Manfred Bernhard; ***Schuler, Gerold***
CS Department of Dermatology, University Hospital of Erlangen, Erlangen, 91052, Germany
SO Journal of Experimental Medicine (2002), 196(6), 867
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
AB The title of the article was incorrect as published originally and an addnl. error was introduced in a correction run in the August 19 issue. The cor. title is given. The title appears correctly in the HTML and PDF versions of the article.

L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:649277 CAPLUS
DN 139:228952
TI Human ***CD4*** + ***CD25*** + regulatory, contact-dependent T cells induce interleukin 10-producing, contact-independent type 10-like regulatory T. cells. [Erratum to document cited in CA137:123934]
AU Dieckmann, Detlef; Bruett, Cord Henrik; Ploettner, Heidi; Lutz, Manfred Bernhard; ***Schuler, Gerold***
CS Department of Dermatology, University Hospital of Erlangen, Erlangen, 91052, Germany
SO Journal of Experimental Medicine (2002), 196(4), 559
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
AB In the title, "Type 1-like" should read "Type 10-like"; the title has been cor.

L13 ANSWER 6 OF 7 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 2
AN 2002262933 EMBASE
TI Human ***CD4*** (+) ***CD25*** (+) regulatory, contact-dependent T cells induce interleukin 1-producing, contact-independent type 1-like regulatory T cells.
AU Dieckmann D.; Bruett C.H.; Ploettner H.; Lutz M.B.; ***Schuler G.***
CS G. Schuler, Dept. of Dermatology, Univ. Hospital of Erlangen-Nuremberg, Hartmannstrasse 14, 91052 Erlangen, Germany. schuler@derma.imed.uni-erlangen.de
SO Journal of Experimental Medicine, (15 Jul 2002) Vol. 196, No. 2, pp. 247-253. .
Refs: 30
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 8 Aug 2002
Last Updated on STN: 8 Aug 2002
AB It has been recently demonstrated that regulatory ***CD4*** (+) ***CD25*** (+) CD45RO(+) T cells are present in the peripheral blood of healthy adults and exert regulatory function similar to their rodent counterparts. It remains difficult to understand how the small fraction of these T cells that regulate via direct cell-to-cell contact and not via secretion of immunosuppressive cytokines could mediate strong immune suppression. Here we show that human ***CD4*** (+) ***CD25*** (+) T cells induce long-lasting anergy and production of interleukin (IL)-10 in ***CD4*** (+) ***CD25*** (-) T cells. These anergized ***CD4*** (+) ***CD25*** (-) T cells then suppress proliferation of syngenic CD4(+) T cells via IL-10 but independent of direct cell contact, similar to the so-called type 1 regulatory T (Tr1) cells. This 'catalytic' function of ***CD4*** (+) ***CD25*** (+) T cells to induce Tr1-like cells helps to explain their central role for the maintenance of immune homeostasis.

L13 ANSWER 7 OF 7 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3
AN 2001207649 EMBASE
TI Ex vivo isolation and characterization of ***CD4*** (+) ***CD25*** (+) T cells with regulatory properties from human blood.
AU Dieckmann D.; Plottner H.; Berchtold S.; Berger T.; ***Schuler G.***
CS G. Schuler, Department of Dermatology, University of Erlangen-Nuremberg, Hartmannstrasse 14, 91052 Erlangen, Germany. schuler@derma.med.uni-erlangen.de
SO Journal of Experimental Medicine, (4 Jun 2001) Vol. 193, No. 11, pp. 1303-1310. .
Refs: 29
ISSN: 0022-1007 CODEN: JEMEAV
CY United States

DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 10 Jul 2001
Last Updated on STN: 10 Jul 2001
AB It has been known for years that rodents harbor a unique population of ***CD4*** (+) ***CD25*** (+) "professional" regulatory/suppressor T cells that is crucial for the prevention of spontaneous autoimmune diseases. Here we demonstrate that ***CD4*** (+) ***CD25*** (+)CD45RO(+) T cells (mean 6% of CD4(+) T cells) are present in the blood of adult healthy volunteers. In contrast to previous reports, these ***CD4*** (+) ***CD25*** (+) T cells do not constitute conventional memory cells but rather regulatory cells exhibiting properties identical to their rodent counterparts. Cytotoxic T lymphocyte-associated antigen (CTLA)-4 (CD152), for example, which is essential for the in vivo suppressive activity of ***CD4*** (+) ***CD25*** (+) T cells, was constitutively expressed, and remained strongly upregulated after stimulation. The cells were nonproliferative to stimulation via their T cell receptor for antigen, but the anergic state was partially reversed by interleukin (IL)-2 and IL-15. Upon stimulation with allogeneic (but not syngeneic) mature dendritic cells or platebound anti-CD3 plus anti-CD28 the ***CD4*** (+) ***CD25*** (+) T cells released IL-10, and in coculture experiments suppressed the activation and proliferation of CD4(+) and CD8(+) T cells. Suppression proved IL-10 independent, yet contact dependent as in the mouse. The identification of regulatory ***CD4*** (+) ***CD25*** (+) T cells has important implications for the study of tolerance in man, notably in the context of autoimmunity, transplantation, and cancer.

=> s Dieckmann, D?/au
L14 100 DIECKMANN, D?/AU

=> s l14 and l1
L15 12 L14 AND L1

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16 6 DUP REM L15 (6 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L16 ANSWER 1 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1
AN 2005289512 EMBASE
TI Activated ***CD4*** (+) ***CD25*** (+) T cells suppress antigen-specific CD4(+) and CD8(+) T cells but induce a suppressive phenotype only in CD4(+) T cells.
AU ***Dieckmann D.*** ; Plottner H.; Dotterweich S.; Schuler G.
CS Dr. G. Schuler, Department of Dermatology, Univ. Hospital of Erlangen-Nuremberg, Hartmannstrasse 14, 91052 Erlangen, Germany. Gerold.Schuler@derma.imed.uni-erlangen.de
SO Immunology, (2005) Vol. 115, No. 3, pp. 305-314. .
Refs: 35
ISSN: 0019-2805 CODEN: IMMUAM
CY United Kingdom
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 21 Jul 2005
Last Updated on STN: 21 Jul 2005
AB ***CD4*** (+) ***CD25*** (+) regulatory T cells are increasingly recognized as central players in the regulation of immune responses. In vitro studies have mostly employed allogeneic or polyclonal responses to monitor suppression. Little is known about the ability of ***CD4*** (+) ***CD25*** (+) regulatory T cells to suppress antigen-specific immune responses in humans. It has been previously shown that ***CD4*** (+) ***CD25*** (+) regulatory T cells anergize CD4(+) T cells and turn them into suppressor T cells. In the present study we demonstrate for the first time in humans that ***CD4*** (+) ***CD25*** (+) T cells are able to inhibit the proliferation and cytokine production of antigen specific CD4(+) and CD8(+) T cells. This suppression only occurs when ***CD4*** (+) ***CD25*** (+) T cells are preactivated. Furthermore, we could demonstrate that CD4(+) T-cell clones stop secreting interferon-.gamma. (IFN-.gamma.), start to produce interleukin-10 and transforming growth factor-.beta. after coculture with preactivated ***CD4*** (+) ***CD25*** (+) T cells and become suppressive themselves. Surprisingly preactivated ***CD4*** (+) ***CD25*** (+) T cells affect CD8(+) T cells differently, leading to reduced proliferation and reduced production of IFN-.gamma.. This effect is sustained and cannot be reverted by exogenous interleukin-2. Yet CD8(+) T cells, unlike CD4(+) T cells do not start to produce immunoregulatory cytokines and do not become suppressive after coculture with ***CD4*** (+) ***CD25*** (+) T cells. .COPYRGT. 2005 Blackwell Publishing Ltd.

L16 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:157515 CAPLUS
DN 140:198100
TI ***CD4*** + ***CD25*** - T cells and Tr1-like regulatory T cells induction and uses thereof in immunosuppression
IN Schuler, Gerold; ***Dieckmann, Detlef***
PA Germany
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1391504	A1	20040225	EP 2002-18025	20020812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004147021	A1	20040729	US 2003-618134	20030711
EP 1391210	A2	20040225	EP 2003-102508	20030812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI EP 2002-18025	A	20020812		
US 2002-419177P	P	20021017		

AB The disclosed invention provides ***CD4*** + ***CD25*** - T cells and Tr1-like regulatory T cells (i.e., contact-independent Type 1-like regulatory T cells), processes for their prodn., and their use for regulatory purposes. The above cells are induced following the co-culture of human ***CD4*** + ***CD25*** + T cells (+/+) with ***CD4*** + ***CD25*** - (+/-) T cells which leads to long-lasting anergy and interleukin-10 formation by +/- T cells. The +/- T cells anergized by the +/+ T cells subsequently suppress the activation of syngeneic CD4+ T cells in an interleukin-10-dependent manner. The +/- T cells or the Tr1-like regulatory T cells can be used for: prepn. of a regulatory medicament; in assays that will allow to identify other regulatory factors; for identifying mols. expressed by the +/- T cells (or the Tr1-like regulatory T cells) including identification of novel mols. on said cells; for identifying precursor cells or progeny of +/- T cells (or the Tr1-like regulatory T cells); and for prepg. an agent for adoptive transfer therapy, an agent for treating immune diseases, or an agent preventing/treating transplant rejections.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:728268 CAPLUS
DN 139:259722
TI Human ***CD4*** + ***CD25*** + regulatory, contact-dependent T cells induce interleukin 10-producing, contact-independent type 1-like regulatory T cells. [Erratum to documents cited in CA137:123934, CA139:228952]
AU ***Dieckmann, Detlef*** ; Bruett, Cord Henrik; Ploettner, Heidi; Lutz, Manfred Bernhard; Schuler, Gerold
CS Department of Dermatology, University Hospital of Erlangen, Erlangen, 91052, Germany
SO Journal of Experimental Medicine (2002), 196(6), 867
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
AB The title of the article was incorrect as published originally and an addnl. error was introduced in a correction run in the August 19 issue. The cor. title is given. The title appears correctly in the HTML and PDF versions of the article.

L16 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:649277 CAPLUS
DN 139:228952
TI Human ***CD4*** + ***CD25*** + regulatory, contact-dependent T cells induce interleukin 10-producing, contact-independent type 10-like regulatory T. cells. [Erratum to document cited in CA137:123934]
AU ***Dieckmann, Detlef*** ; Bruett, Cord Henrik; Ploettner, Heidi; Lutz, Manfred Bernhard; Schuler, Gerold
CS Department of Dermatology, University Hospital of Erlangen, Erlangen, 91052, Germany
SO Journal of Experimental Medicine (2002), 196(4), 559
CODEN: JEMEAV; ISSN: 0022-1007
PB Rockefeller University Press
DT Journal
LA English
AB In the title, "Type 1-like" should read "Type 10-like"; the title has been cor.

L16 ANSWER 5 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 2
AN 2002262933 EMBASE
TI Human ***CD4*** (+) ***CD25*** (+) regulatory, contact-dependent T cells induce interleukin 1-producing, contact-independent type 1-like regulatory T cells.
AU ***Dieckmann D.*** ; Bruett C.H.; Ploettner H.; Lutz M.B.; Schuler G.
CS G. Schuler, Dept. of Dermatology, Univ. Hospital of Erlangen-Nuremberg, Hartmannstrasse 14, 91052 Erlangen, Germany. schuler@derma.imed.uni-erlangen.de
SO Journal of Experimental Medicine, (15 Jul 2002) Vol. 196, No. 2, pp. 247-253. .
Refs: 30
ISSN: 0022-1007 CODEN: JEMEAV
CY United States

DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 8 Aug 2002
Last Updated on STN: 8 Aug 2002
AB It has been recently demonstrated that regulatory ***CD4*** (+) ***CD25*** (+) CD45RO(+) T cells are present in the peripheral blood of healthy adults and exert regulatory function similar to their rodent counterparts. It remains difficult to understand how the small fraction of these T cells that regulate via direct cell-to-cell contact and not via secretion of immunosuppressive cytokines could mediate strong immune suppression. Here we show that human ***CD4*** (+) ***CD25*** (+) T cells induce long-lasting anergy and production of interleukin (IL)-10 in ***CD4*** (+) ***CD25*** (-) T cells. These anergized ***CD4*** (+) ***CD25*** (-) T cells then suppress proliferation of syngenic CD4(+) T cells via IL-10 but independent of direct cell contact, similar to the so-called type 1 regulatory T (Tr1) cells. This 'catalytic' function of ***CD4*** (+) ***CD25*** (+) T cells to induce Tr1-like cells helps to explain their central role for the maintenance of immune homeostasis.

L16 ANSWER 6 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3
AN 2001207649 EMBASE
TI Ex vivo isolation and characterization of ***CD4*** (+) ***CD25*** (+) T cells with regulatory properties from human blood.
AU ***Dieckmann D.*** ; Plottner H.; Berchtold S.; Berger T.; Schuler G.
CS G. Schuler, Department of Dermatology, University of Erlangen-Nuremberg, Hartmannstrasse 14, 91052 Erlangen, Germany. schuler@derma.med.uni-erlangen.de
SO Journal of Experimental Medicine, (4 Jun 2001) Vol. 193, No. 11, pp. 1303-1310. .
Refs: 29
ISSN: 0022-1007 CODEN: JEMEAV
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 10 Jul 2001
Last Updated on STN: 10 Jul 2001
AB It has been known for years that rodents harbor a unique population of ***CD4*** (+) ***CD25*** (+) "professional" regulatory/suppressor T cells that is crucial for the prevention of spontaneous autoimmune diseases. Here we demonstrate that ***CD4*** (+) ***CD25*** (+)CD45RO(+) T cells (mean 6% of CD4(+) T cells) are present in the blood of adult healthy volunteers. In contrast to previous reports, these ***CD4*** (+) ***CD25*** (+) T cells do not constitute conventional memory cells but rather regulatory cells exhibiting properties identical to their rodent counterparts. Cytotoxic T lymphocyte-associated antigen (CTLA)-4 (CD152), for example, which is essential for the in vivo suppressive activity of ***CD4*** (+) ***CD25*** (+) T cells, was constitutively expressed, and remained strongly upregulated after stimulation. The cells were nonproliferative to stimulation via their T cell receptor for antigen, but the anergic state was partially reversed by interleukin (IL)-2 and IL-15. Upon stimulation with allogeneic (but not syngeneic) mature dendritic cells or platebound anti-CD3 plus anti-CD28 the ***CD4*** (+) ***CD25*** (+) T cells released IL-10, and in coculture experiments suppressed the activation and proliferation of CD4(+) and CD8(+) T cells. Suppression proved IL-10 independent, yet contact dependent as in the mouse. The identification of regulatory ***CD4*** (+) ***CD25*** (+) T cells has important implications for the study of tolerance in man, notably in the context of autoimmunity, transplantation, and cancer.

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